

Presumed Combined Brilliant Blue G and Endolight-Induced Macular Damage following Epiretinal Membrane Removal Surgery

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Abstract

Purpose: To report a rare case of macular outer retinal and retinal pigment epithelium (RPE) damage following brilliant blue G (BBG)-assisted epiretinal membrane (ERM) removal surgery.

Methods: Retrospective, observational case report.

Results: An 85-year-old lady presented with decreased vision in the left eye and a best-corrected visual acuity of 20/400. The right eye examination was within normal limits. The left eye had a significant cataract, and the fundus examination through the cataractous haze showed an ERM with macular pucker, which was confirmed on an optical coherence tomography (OCT) scan. A combined cataract surgery with intraocular lens implantation and BBG-assisted ERM removal and internal limiting membrane peeling surgery was performed. Over the subsequent visits, a well-defined area of outer retinal and RPE alteration was identified on OCT and fundus autofluorescence without significant improvement in visual acuity. At the last follow-up visit, the visual acuity minimally improved to 20/200.

Conclusions: Macular toxicity due to repeated usage of BBG dye and high intensity focal endo-illumination may lead to poor visual outcome following ERM removal or similar macular surgeries. Adequate precautions need to be taken to prevent vision loss.

Keywords: Brilliant blue G, Epiretinal membrane, Phototoxicity, Retinal damage, Surgery

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INTRODUCTION

The indications for epiretinal membrane (ERM) removal include the presence of retinal traction along with disabling metamorphopsia and/or reduced visual acuity.¹ Performing surgery for ERM is associated with retinal complications such as intraoperative hemorrhage, retinal tears leading to detachments, macular edema, and recurrent ERM.² Another important problem following ERM removal surgery includes the development of recurrent ERMs. The reasons for recurrent ERMs include incomplete ERM removal and/or the persisted

internal limiting membrane (ILM) after ERM peeling, even though the ERM seems to have been completely peeled.³ Therefore, ILM peeling not only reduces the likelihood of re-proliferation of ERM but also seems to improve the visual prognosis of recurrent ERMs.⁴

In recent years, the intravitreal application of brilliant blue G (BBG) has gained popularity to visualize the ILM.⁵ As against indocyanine green and trypan blue, BBG has shown to have a good safety profile providing satisfactory

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anatomical and functional postoperative results.⁶ However, in recent literature, there are a few reports of outer retinal layer and retinal pigment epithelium (RPE) damage following BBG-assisted macular hole surgeries due to seepage of BBG dye through the macular hole into the subretinal space.^{7,8} This is unlikely to happen in ERM removal surgery.

In this report, we describe an unusual case of macular toxicity presumably occurring within a short interval following BBG-assisted ERM and ILM peeling. To the best of our knowledge, this appears to be the first report to describe outer retinal and RPE layer damage following BBG-assisted ERM removal surgery on PubMed search.

CASE REPORT

An 85-year-old lady was referred from the cataract clinic for precataract surgery retinal evaluation. Her presenting visual acuity in the right eye was 20/100 and the left eye was 20/400, respectively. The anterior segment examination and intraocular pressure in both eyes were normal. The density of cataract in both eyes was nuclear sclerosis grade 4. Fundus examination through the hazy media due to cataract revealed an ERM with a macular pucker in the left eye. The right eye fundus examination was normal. Spectral-domain optical coherence tomography (OCT) using the Spectralis Heidelberg machine confirmed a grade 4 ERM with prominent thickening of the inner retinal layers in the left eye [Figure 1a]. The visible outer retinal and RPE layers beyond the extent of the ERM appeared normal. A combined cataract surgery and ERM removal surgery were recommended which she underwent 3 days after presentation. After performing the cataract surgery, a 25-gauge, 3-port pars plana vitrectomy using the Alcon, CONSTELLATION® Vision System was performed. After core vitrectomy, intravitreal triamcinolone acetonide was injected to stain the posterior cortical vitreous. The posterior vitreous detachment was completed. Fluid air exchange was done. ILM was stained using BBG (Ocublue Plus 0.05%w/v, Aurolab) for a contact time of 2 min. After 2 min, excess BBG was removed passively with flute needle and saline infusion was started. A negative ERM staining and positive ILM staining were achieved. The ERM was firmly adherent to the underlying retinal tissue and was peeled with difficulty in a piecemeal manner using the disposable GRIESHABER® asymmetrical forceps using the pinch-pick-n-peel technique. After ERM peeling, it was decided to restrain the ILM with BBG under air. Again, a contact time of 2 min was given. ILM peeling was achieved in a uniform manner. Residual retinal folds were noted after ILM peeling. The duration of ERM and ILM peeling was prolonged and the total retinal surgery duration was 50 min. No other complications were noted intraoperatively and fluid-air exchange was done at the end of the surgery. The entire surgery was performed at a high endolight intensity (115%).

On postoperative day 1, the anterior segment and intraocular pressure were normal. Retina appeared attached through the

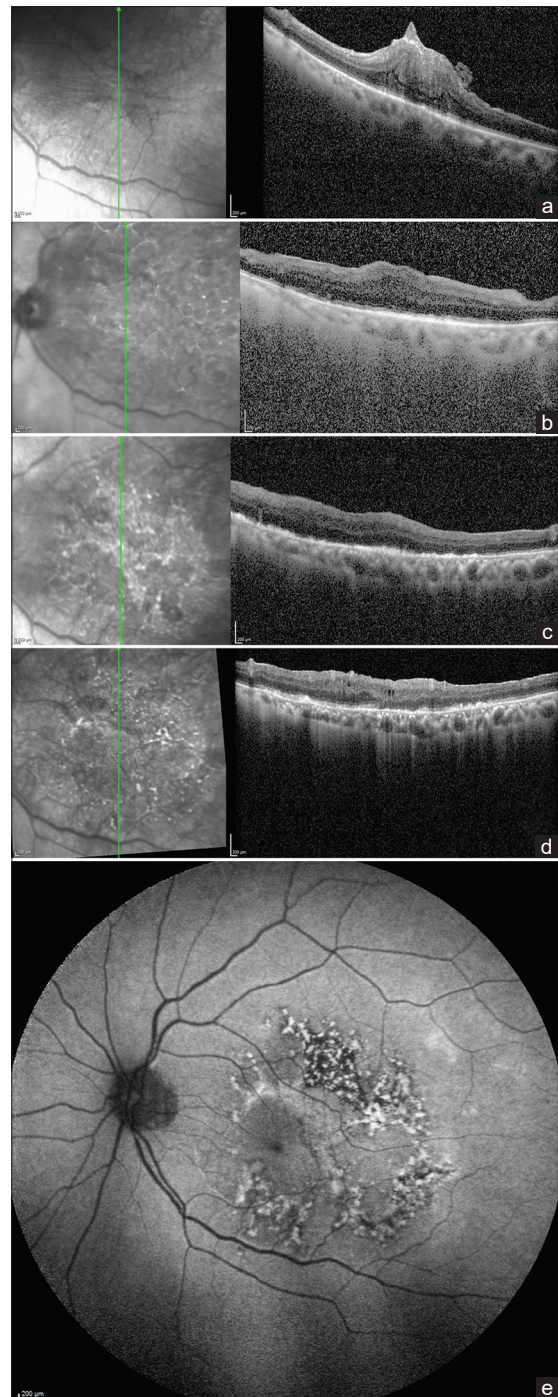


Figure 1: Optical coherence tomography (OCT) and fundus autofluorescence (FAF) images of the left eye: (a) At presentation, there is a thick grade 4 epiretinal membrane (ERM) with prominent thickening of the inner retinal layers on OCT (retinal thickness = 598 μ m). The outer retina layers and retinal pigment epithelium (RPE) layer visible beyond the extent of the ERM appear to be normal on OCT. (b-d) OCT images at 1-week, 4-week, and 4-month postsurgery, respectively show the damaged retinal pigment epithelial and outer retinal layers. There is a progressive reduction of inner retinal layer thickening over time (postoperative visit at 1-week = 428 μ m, at 4-week = 321 μ m, and 4-month = 270 μ m). In the areas of RPE damage, choroidal vessels and choriocapillaris thinning were clearly noted on OCT scans. (e) FAF of the left eye showing a well-defined area of mixed autofluorescence pattern confirming the damaged outer retinal and RPE layers

air bubble. Other macular findings were not clearly made out and were difficult to comment on. After 1 week, the visual acuity documented was 20/200 in the left eye. Fundus examination showed a pale-looking retina at the posterior pole and OCT showed reducing inner retinal thickening with disrupted outer retinal and RPE layers [Figure 1b]. In the areas of RPE damage, choroidal vessels and choriocapillaris thinning were clearly noted on OCT scans. Residual air bubble (40%) was present. At her next follow-up visit after 4 weeks, the patient was unhappy with her vision. Her vision in the left eye remained at 20/200 and OCT showed a reduction in the retinal thickening with damaged outer retinal and RPE layers [Figure 1c]. At the last follow-up visit 4 months after surgery, OCT still showed damaged outer retinal layers and abnormal RPE layer, further reduction in retinal thickness and visual acuity documented was still 20/200 [Figure 1d]. Fundus autofluorescence (FAF) showed areas of hypo- and hyperautofluorescence suggestive of damaged RPE and outer retinal layers [Figure 1e]. Informed consent was obtained from the patient for publication purpose.

DISCUSSION

Over the years, double staining of ILM with BBG followed by ILM peeling in cases with ERM has been a well-accepted technique to prevent ERM recurrence.^{9,10} Our case highlights the occurrence of retinal pigment epitheliopathy and outer retinal layer damage along with sparing of inner retinal layers occurring as early as 1 week following BBG-assisted ERM peeling in grade 4 ERM. We also note the changes on OCT and FAF over 4 months.

Several possibilities could be considered to explain the RPE and photoreceptor layer damage in our case. This could have occurred either due to the direct trauma to the Müller cells, phototoxic damage to the retina, or could be related to the vital dye-related toxicity and toxicity due to the inappropriate antibiotic dose in the saline infusion.

Direct mechanical trauma may occur during the creation of the initial flap of membrane with the forceps, but it is usually limited to the site of contact. Furthermore, difficult peeling in firmly adherent ERM can cause mechanical damage to the Müller cell footplate. Endoilluminator-related toxic maculopathy has also been described by several reports and is associated with increased surgical time, prior fundus pigmentation, increased exposure to light, and less distance between the endoilluminator and retina.^{7,8} Our previous case report documented the role of endoilluminator and BBG dye in causing outer retinal damage following a macular hole surgery.⁷ At the last follow-up visit 2 years after the surgery, there was no significant structural improvement on OCT and FAF and the visual acuity remained at 20/320. In this case, there was no prior fundus pigmentation and the surgical time was prolonged (50 min), with standard procedure technique and no intraoperative complications. The CONSTELLATION® Vision System from Alcon uses the

xenon light for endoillumination during vitreoretinal surgeries. Xenon light has a peak wavelength of 450 nm (range, 420–700 nm).¹¹ The increased absorption of the xenon light in the presence of BBG causes changes in the BBG emission spectra which produce toxic-free radicals and subsequent damage to the RPE cells and photoreceptors. Studies on the human RPE cells (ARPE-19) have shown that RPE cell viability to reduce in the presence of BBG when high focal illumination is used for >5 min and diffuse medium illumination is used for >15 min, respectively.¹² In this case, double ILM staining with BBG under air for a longer duration (2 min in this case), longer surgical time due to difficult ERM and ILM peeling, and also probably ending the case with air in the vitreous cavity, thereby causing the entrapment and retention of BBG molecules in the eye for a longer time could have contributed to the RPE and outer retinal damage and poor visual outcome. What is different in our case is the absence of direct exposure of the RPE to the BBG dye and the light energy of the endolight. This case also warns us of the possible outer retinal and RPE damage following the BBG-assisted macular surgeries in the absence of a macular hole.

In conclusion, we describe a rare case of macular toxicity may be due to BBG and high-intensity focal endoillumination following ERM removal surgery. This report instructs the retinal surgeon to be quick and precise while performing macular surgeries and to avoid repeated ILM staining with BBG under air, preferably ≤ 1 min. Furthermore, one should avoid the use of high-intensity focal illumination close to the macula to avoid any phototoxic damage to the RPE cells and photoreceptors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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